

Please replace the first full paragraph on page 3 with the following:

In another embodiment of this bioactive aspect of the biomolecular interaction, where the carrier may also be bioactive, the carrier provides controlled release of the biologically active biomolecular interaction over time.

Please replace the third full paragraph on page 3 with the following:

In another aspect of the invention there are provided methods of preparing the carrier and the biomolecular interaction incorporated in the carrier.

Please replace the third full paragraph on page 4 with the following:

According to yet another embodiment the partial drying is at temperatures from about 4° to about 40°C.

Please replace the fourth full paragraph on page 4 with the following:

In another aspect of the invention there is provided a method for the preparation of a carrier having a bioactive biomolecular interaction incorporated in the carrier.

Please replace the last full paragraph on page 4 with the following:

According to one embodiment of this aspect, the method comprises:

- (a) incorporating the bioactive biomolecular interaction in a carrier;
- (b) hydrolysis and polycondensation of at least one monomer to provide a solid matrix bonding the bioactive biomolecular interaction which is incorporated in the carrier ; and
- (c) imparting mechanical, chemical and thermal stability in the matrix.

At page 5, please replace the fourth full paragraph with the following:

In yet another aspect of the invention there is provided a method of treating an animal with a carrier and a biomolecular interaction of the invention. According to one embodiment the method comprises administering an effective amount of a biologically active biomolecular interaction contained in a carrier such that the animal is thereby treated. Preferably the

treating is by site-specific targeting in the animal. More preferably the effective amount of a biologically active biomolecular interaction is a chemotherapeutic for treating cancer.

Please replace the paragraph bridging pages 6 and 7 with the following:

According to another broad aspect the invention provides materials and methods of high throughput screening for compounds or substances which inhibit protein-protein interactions, but as will readily be appreciated, the methods and materials described herein may be used to assay any substance-substance interactions. In this respect the invention provides a method of high throughput screening for a substance which inhibits or binds a biomolecular interaction. According to an embodiment of this aspect of the invention the method comprises the steps of:

(a) incorporating a biomolecular interaction within a carrier. Preferably the biomolecular interaction is a population of a purified protein comprising a binary protein-protein interacting pair is encapsulated in a carrier. This protein is preferably designed so that it has a solvent-sensitive fluorescent probe at or near the dimer interface or has one protein partner labelled with a fluorescence energy donor and the other protein partner labelled with a fluorescence energy acceptor to allow fluorescence resonance energy transfer (FRET) to occur between the protein partners, preferably in a distance-dependent manner.

(b) forming an array of sol-gel derived spots on a support wherein each spot contains a biomolecular interaction;

(c) measuring a signal from the interaction in the absence of any other substances; Preferably the initial fluorescence signal (intensity, emission wavelength, polarization and/or lifetime of a single probe, a donor and/or an acceptor) of this complex in the absence of any other compounds is first measured. The fluorescence signal indicates that the pair of proteins is in a complex.

(d) reversibly disrupting the biomolecular interaction such that the signal is detectably altered; Preferably the sample is sufficiently denatured (if necessary) to cause a reversible disruption of the binary protein-protein interaction, causing the signal of the reporter at the protein-interface or of the donor-acceptor pair to be significantly altered.

(e) the substance is added to the biomolecular interaction in the carrier, and reversing the disruption; and

(f) measuring the signal; The denaturing conditions (if used) are reversed to cause the binary interacting system to reform in the sol-gel matrix. The original fluorescence signal of the attached probe or donor-acceptor pair is recovered if no disruption of the complex occurs (i.e., target is not a drug candidate). Where the original signal is not recovered, the substance is determined to bind or inhibit the biomolecular interaction. The substance is considered to have disrupted the protein-protein interaction, and can be tested further as, for example, a potential drug candidate.

At page 7, please replace the first full paragraph with the following:

In a preferred embodiment the signal generated by the assay is due to excitement by a He Cd laser through an optical fiber and the signal, preferably fluorescence, and is preferably detected through the same fiber, as shown in Figure 21.

At page 10, please replace the first full paragraph with the following:

As used herein, the expression "interfere with" and like expressions mean inhibiting, reducing, diminishing or blocking the interaction between the members of a biomolecular interaction.

At page 10, please replace the second full paragraph with the following:

The term "interaction" as used herein means the binding, association, or complexing of the members of a biomolecular interaction and includes intramolecular binding, association or complexing, regardless of the degree of association between molecules, or intra molecularly, however the association is formed.

At page 10, please replace the sixth full paragraph with the following:

The term "containing" as used herein means any form or type of integration, or incorporation such that the substance or substances, including biomolecular interaction, is/are able to be carried by a carrier.

At page 22, please replace the second full paragraph with the following:

The invention contemplates a method for screening a compound to determine the degree of inhibition or stimulation (i.e. binding) of a biomolecular interaction by the compound, or if it interferes with the biomolecular interaction. The method involves contacting a compound to be tested with molecules of a biomolecular interaction incorporated within a carrier as described herein. The molecules are preferably not complexed but are capable of forming a biomolecular interaction in the carrier. Therefore, a method of the invention may initially involve disrupting a biomolecular interaction by applying a denaturant (e.g. temperature, pH, or urea). The denaturation of the interaction may be achieved using a cyclic denaturation (temperature, urea, or pH cycling). The screening method is carried out under conditions suitable for the formation of a biomolecular interaction. The conditions are selected having regard to factors such as the nature of the molecules forming the interaction. In a preferred method of the invention the carrier is a silica based glass, most preferably a sol-gel derived glass. The biomolecular interaction within a carrier is preferably cast on the surface of an optical fiber, planar supports (waveguides), a slide, a microtiter well or an array of sol-gel derived spots formed by pin spotting, stamping, inkjet deposition or screen printing.

Please replace the first full paragraph on page 33 with the following:

Once it was determined that reversible denaturation of the entrapped complex was possible, we examined the ability of a known inhibitor of the complex, trifluoperazine (TFP), to disrupt the complex. Control experiments involved an examination of the interactions of TFP with the intact complex, melittin, BCaM, and non-functional complex, obtained using apo BCaM. Interaction of TFP with apo or holo calmodulin alone resulted in no changes in spectroscopic properties. The interaction of TFP with melittin and with the intact BCaM:melittin complex are shown in Figures 10A and 10B. Note that no wavelength changes occurred during this titration (not shown).